ODN (18mer) was injected with the PB (n = 7) at 4 atm inflation pressure for 30 s: with the IO (n = 3) ODN was applied with 7.5 mA current for 3 × 60 s. Parallel studies were performed using rhodamine labelled ODN (rhoODN) for histological localization. Samples were harvested at 30 min, 2 h, 24 h and 7 d and processed for scintillation counting or fluorescence microscopy.

Results:

		μg ODN per artery			
		30 min	2 hours	24 hours	7 days
PB	570 μg/ml	3.45 ± 1.3	1.42 ± 0.65	0.08 ± 0.02	ND
IO	855 μg/ml	7.3 ± 2.4	1.5 ± 0.6	0.52 ± 0.35	0.26 ± 0.11

n = 3/group; data are mean ± SEM

While IO appeared to deliver more than PB acutely, there was rapid washout at 2 h in both groups. However, after 24 h persistence appeared better with the IO, and in one sample there was persistence at 7 d with IO. This may have been in part due to improved tissue distribution and cellular uptake with IO, which was detected with rhoODN.

Conclusion: Iontophoresis appears superior to PB for LD of ODN in pig coronary arteries and may be feasible for restenosis prevention in the clinical setting.

938-38 Acute Arterial Occlusion and Platelet Deposition Are Markedly Reduced by Local Delivery of a Novel Nitric Oxide Donor

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Nitric oxide (NO) is an endothelial-derived vasodilator and anti-platelet aggregation factor. We studied local delivery of a novel NO donor in pigs after severe carotid artery crush injury. *In vivo* quantitative platelet deposition (PD) was measured by 111-In tropolone labeled platelets, and normalized blood flow (NBF) measured by Doppler flowmetry. Local arterial infusion of the NO donor dansylpiperazine nonoate (GLO/NO) was compared with control (saline), infused identically by the Dispatch catheter. Four groups were studied: *A* (10 arteries): injury, local saline, *B* (10 arteries): injury, local GLO/NO (10 ml/3 × 10^{-4} mol over 10 min), *C* (9 arteries): injury, systemic GLO/NO (3 × 10^{-4} mol), *D* (6 arteries): injury, systemic GLO/NO, local saline. Each was studied at 1 and 24 hours.

Group	A		B		C		D	
Time (hr)	1	24	1	24	1	24	1	24
Patency (%)	80	60	90*	90#	33*	11#	83	66
NBF	0.25*	0.26*	0.73*	0.75*	0.18*	0.07*	0.59	0.13
PD (× 10^5/cm^2)	5.5 ± 2.2*		1.3 ± 0.4*		4.9 ± 1.0*		7.6 ± 3.1	

*p < 0.05: Group A vs B, Group B vs C, #p < 0.005: Group B vs C

Conclusion: Local NO delivery significantly reduces occlusion and platelet deposition after severe arterial injury. This underscores the role of NO as a modulator of vascular tone and thrombus formation, and suggests an effective therapeutic strategy following angioplasty.

938-39 In Vitro Model to Investigate Stent Activated Platelets by Flow Cytometry

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The application of stents in coronary arteries is still limited by acute or subacute occlusion. Activated platelets play a major role in thrombus formation. In an in vitro model of stent thrombosis we investigated the expression of activation dependent glycoproteins (GP) on platelets by flow cytometry. Tantalum wire stents (n = 12) were placed in one of two parallel silicon tubings with circulating citrated platelet rich plasma of healthy and drug free volunteers. Over 10 minutes aliquots of platelet rich plasma were drawn via a three way faucet in two minute intervals. Blood samples were immediately fixed with glyoxal, paraformaldehyde and buffer. For flow cytometric analysis monoclonal antibodies CD41a (GPIIb/IIIa), CD42b (GPIb), CD62 (GMP-140) and CD63 (GP53) were used. 10,000 events were acquired in a life gate setting. Results were expressed as "platelet activation" (PA; Rinder, Transfusion 33, 1993). Within 2 minutes after the start of circulation, the expression of CD62 and CD63 increased in the tubing system with the stent. Over 10 minutes platelet activation progressively increased; CD62 1051 ± 548 vs 359 ± 358 PA control without stents ($p < 0.01$) and CD63 981 ± 355 vs 428 ± 156 PA ($p < 0.005$). Antigens CD41a and CD42b did not show significant changes. Thus, in our in vitro model there is activation of platelets by stents probably caused by shear stress and contact to the artificial surface. Flow cytometry is a diagnostic tool to quantify platelet activation, and may help to improve stent material and design.

938-40 Photodynamic Therapy and Local Drug Delivery in a Restenosis Model

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Photodynamic therapy (PDT) was examined in porcine restenosis model. Unidirectional injury of media by a atherectomic catheter (UI) was used. The photosensitizer, Photofrin (PF; QLT, Canada) was delivered with a new needle injection catheter (NIC) and activated by adequate monochromatic light irradiation. 46 arterial segments from pigs (mean weight 34 kg) underwent UI and were removed at 7, 14 or 21 days. 16 vessel segments received no further treatment (Group 1); 12 segments received UI and local drug delivery or monochromatic light exposure. (Group 2 and 3) 28 segments underwent UI followed by selective application of 5 mg PF per treated segment and exposure to monochromatic light with a light delivery catheter (630 nm) with 100 J/cm2 (Group 4, therapeutic group). All vessels were explanted and processed for immunohistochemistry and electron microscopy.

Group 1: An intense inflammation with polymorphonuclear leukocytes and subsequent proliferation of myofibroblasts (maximum after 7 d) was found. After substantial vessel injury only (Group 1), a myoproliferative response resulted in tissue hyperplasia of 1.8 ± mm^2. Group 2 and 3 results did not reveal significant differences to group 1. In media-injured vessels treated with PDT, no inflammation and or proliferative response resulted (area of tissue hyperplasia 0.3 mm^2). A marked destruction of nuclear membranes with PF deposits in smooth muscle cells with cytoplasmatic vacuoles were seen after PDT. These results were only seen with laser application after PF delivery. There were no alterations in nuclear morphology.

Thus, after selective application of a photosensitizer, local PDT led to a marked reduction of proliferation and tissue hyperplasia in a porcine model of restenosis without adverse effects.

938-41 Efficiency of Coronary Drug Delivery With the Needle Injection Catheter

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Local delivery of antiphlogistic/proliferative agents might prevent or protract restenosis development. To date local drug delivery is hampered by low local efficiency and adjacent tissue contamination. A new designed over-the-wire needle injection catheter (NIC) for coronary application was used. C^{14}-labelled Carvedilol (molecular weight 400) or Benzoporphyrinderivative (BPD) was tested in normal coronary and femoral porcine arteries (n = 19). The NIC system was used for drug delivery of either 0.3 mg or 0.03 mg C^{14}-Carvedilol (Group 1) or 2 mg BPD (Group 2). Vessels were removed up to 4 hours after drug delivery. Determination of drug content was performed after homogenisation of vessel tissue in ascintillation counter (combustion) or by chromatography. There were no significant differences in the results between 0.3 mg or 0.03 mg C^{14}-Carvedilol or in the analyzation methods (Group 1 or 2). The maximum content could be detected at 2 hours (14.2 ± 1.2% of total drug amount) in perivascular tissue (media 1–2.5%) with a decrease thereafter (to 2.9 ± 01%). There was contamination of perivascular tissue, as ascertained by enhanced drug content (maximum 0.39% of total drug amount immediately after drug delivery). No systemic content was measured after local drug delivery with the NIC; there was no measurable renal, hepatic or splenic drug content.

In conclusion, local drug delivery into arterial vessel wall is feasible using the new needle injection catheter system. It allows a higher efficiency, with prolonged delivery compared with data available relating to other local drug delivery systems. Adjacent tissue contamination must be taken into consideration.

938-42 Local Delivery of Lipid-Complexed Oligonucleotide to Balloon-Injured Pig Coronary Arteries: Radiolabelling Pharmacokinetic and Correlative Fluorescence Microscopic Analysis

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Localized delivery (LD) of conventional drugs, gene constructs, and oligonucleotides (ODN) is a potential means to prevent iatrogenic restenosis and thrombosis after vascular interventions. Problems with this technology in-